Supplementary Discussion

Protein-protein Interactions

PPIs can also occur between ordered segments. The amyloid beta precursor protein is a receptor helping neurite growth and neuronal adhesion. The structure of the E2 domain of the protein was solved multiple times, both in dimeric [1] and monomeric [2] forms, suggesting the domain is stable in both forms. It was proposed that dimerization aids the masking of several sites with biological activity [3], and thus the oligomerization state may regulate fibroblast growth by hiding a short sequence motif (RERMS), which was shown to promote growth processes [4].

A particular case of domain-domain interaction is the complex formation by transmembrane (TM) proteins. Membrane proteins often assemble into higher-order complexes to mediate transport or signaling. Nicotinic acetylcholine receptors are ion channels assisting fast chemical neurotransmission with high functional diversity, assembling into a pentameric form. Monomers consist of four TM helices, and the complex has an inner ring of helices, shaping the pore, while the outer three helices of each monomer shield the inner rings from lipids. In the closed state, the inner helices are in proximity and gate the channel. Upon acetylcholine binding, a conformational change occurs: the individual TM subunits remain rigid, however, the arrangement of the channel changes to become permeable for sodium ions [5].

An interesting, however somewhat logical aspect of the TM proteome of PSD is the underrepresentation of different GPCR proteins, otherwise constituting the most abundant protein family [6]. Over half of GPCRs encode olfactory receptors, responsible for perceiving a high variety of chemicals. Cell-cell communication relies on receptors, however, the highly specialized ways of synaptic transmission may not require to distinguish such a diverse range of ligands as olfactory perception.

A more direct way to modulate PPIs is the control of the presence of its components at specific locations. Although it is hard to asses large scale protein synthesis and expression level data, ubiquitination sites hint the possibility of proteasome activity and degradation. It was shown that blocking either the synthesis or the degradation of synaptic proteins impairs the maintenance of late-phase long-term potentiation (L-LTP), however simultaneous blockade of protein degradation and protein translation leads to the rescue of L-LTP [7], suggesting an important role of ubiquitination in the PSD.

Supplementary Figures

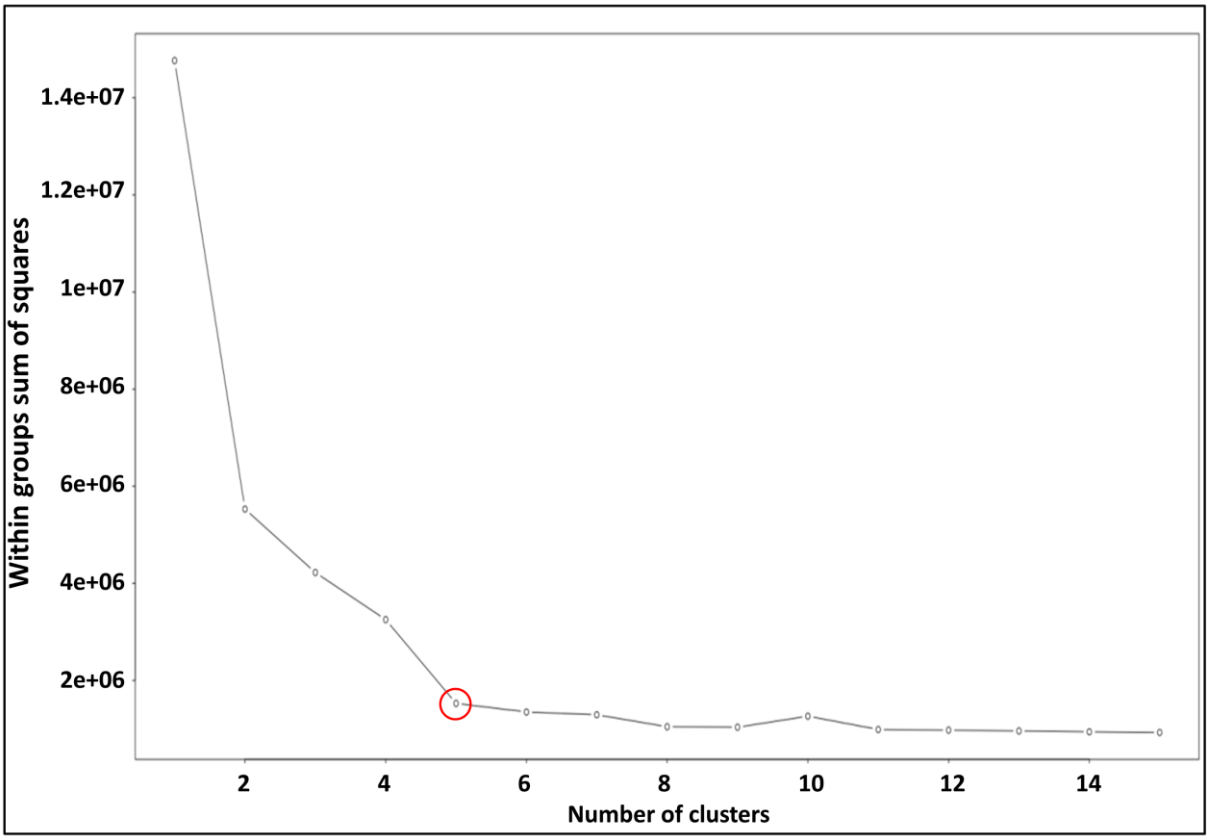

Figure S1: K-means evaluation of various numbers of clusters of AAIndex.

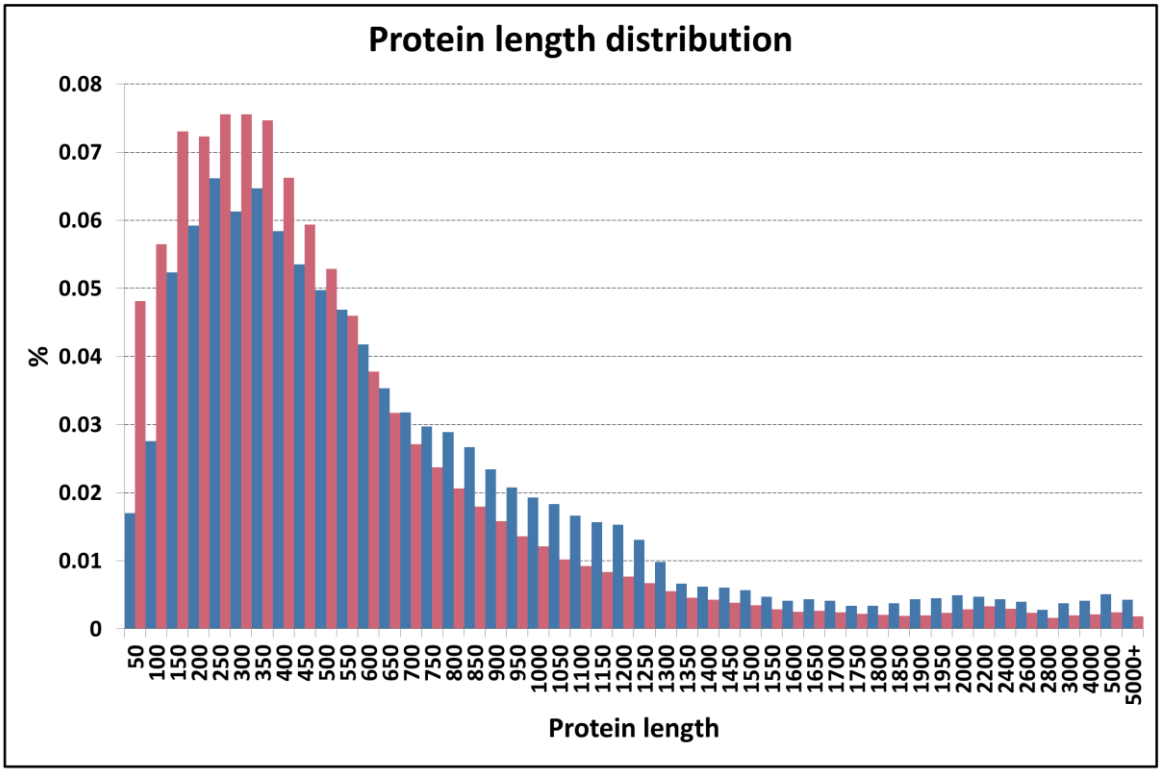

Figure S2: Protein length distribution (blue: PSD, red: human proteome)

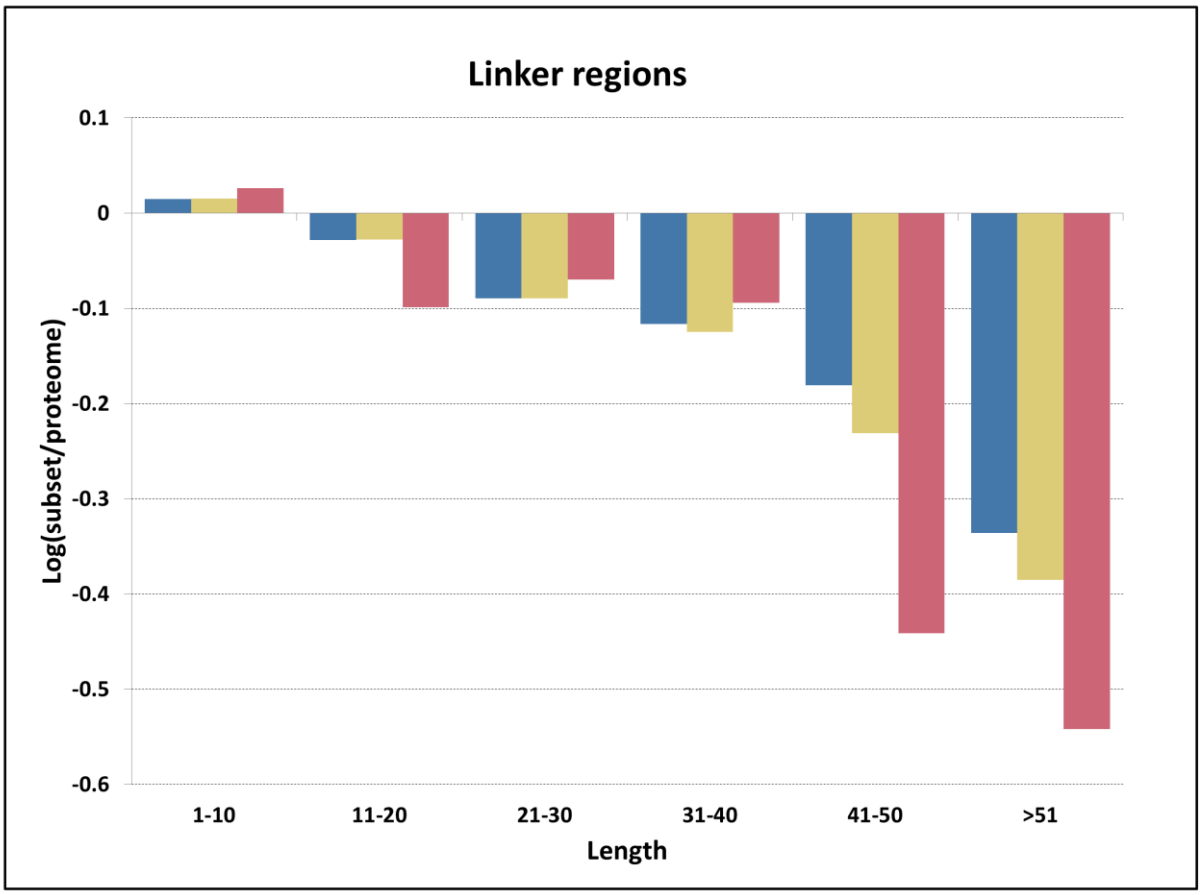

Figure S3: Flexible linker length distribution compared to the human proteome (blue: synaptome, yellow: PSD, red: PSC)

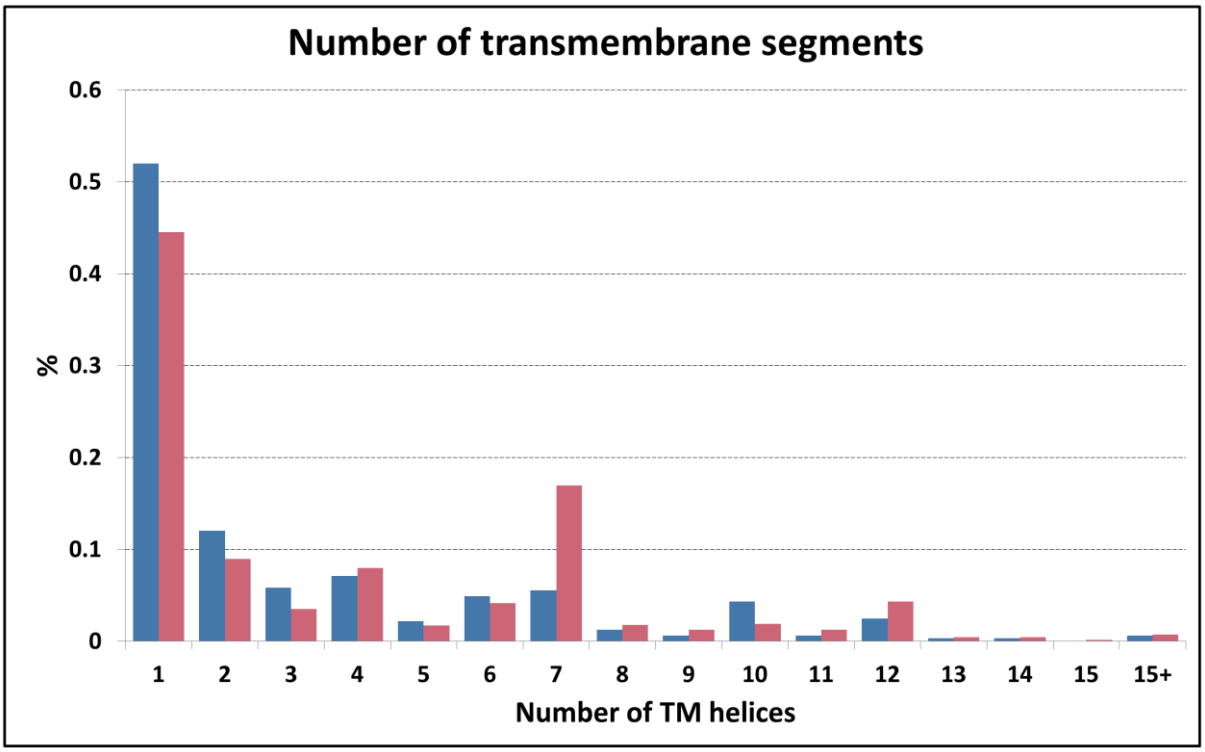

Figure S4: Transmembrane helix distribution (blue: PSD, red: human proteome)

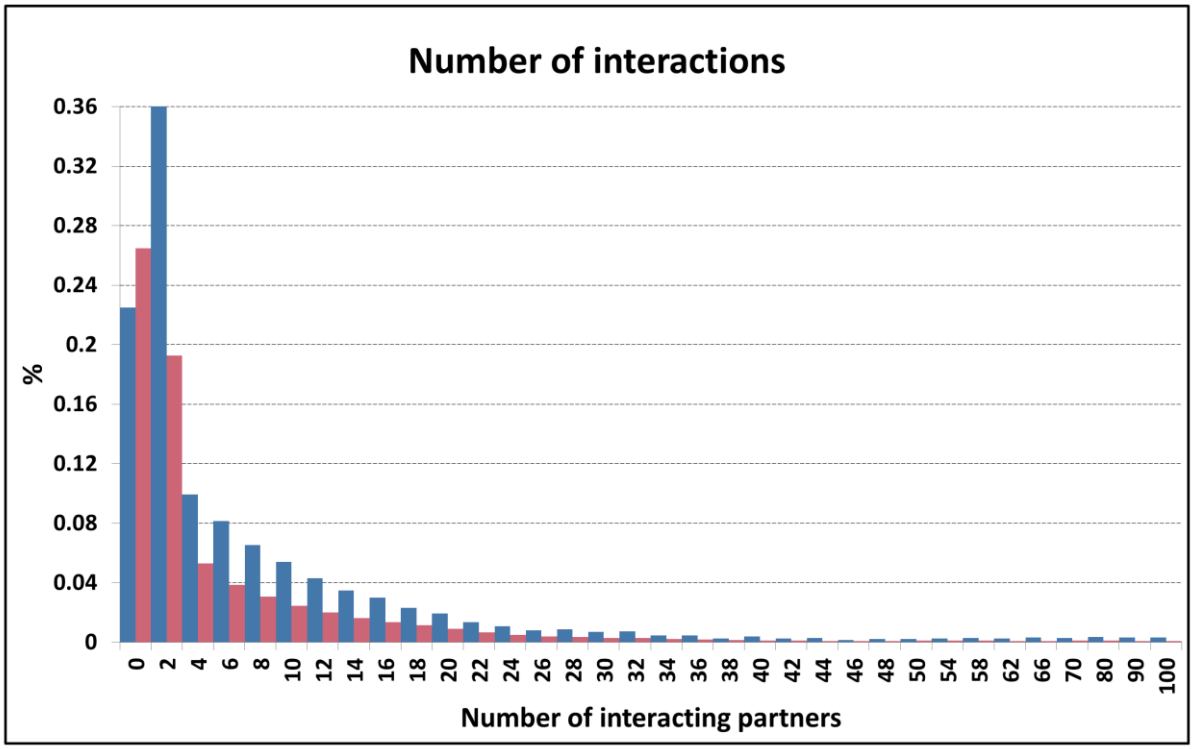

Figure S5: Distribution of the number of interacting partners (blue: PSD, red: human proteome)

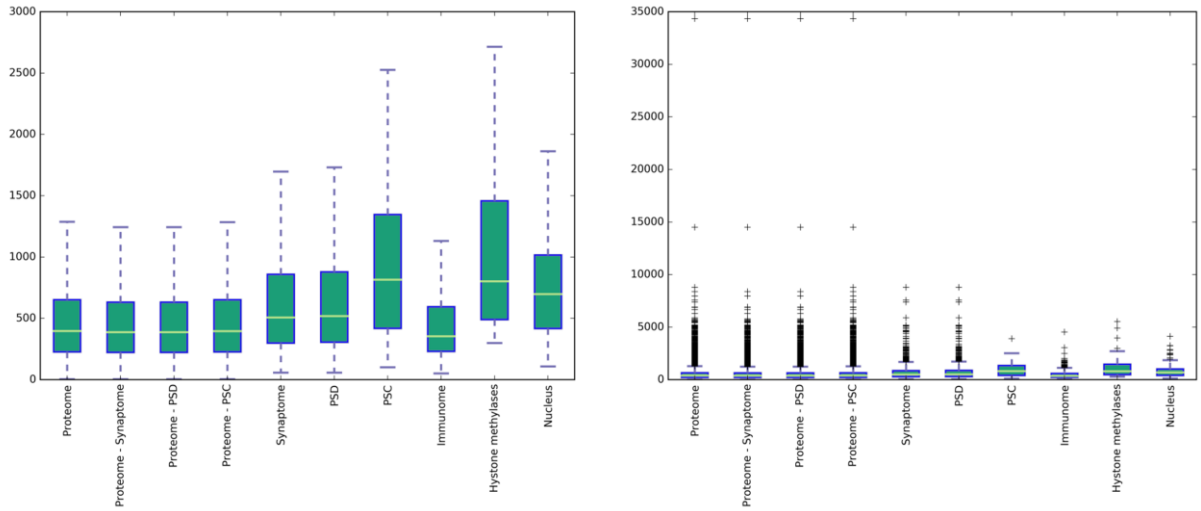

Figure S6: Boxplot of protein lengths in all datasets (left: without data points; right: with outlier data points. Note the different y-axes).

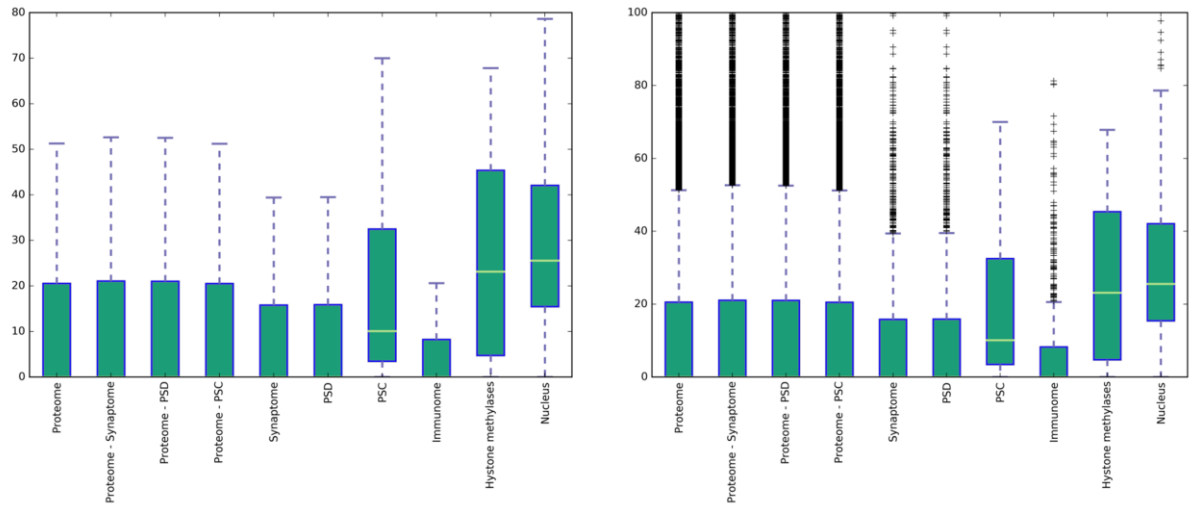

Figure S7: Boxplot of intrinsically disordered residue content in all datasets (left: without data points; right: with outlier data points. Note the different y-axes).

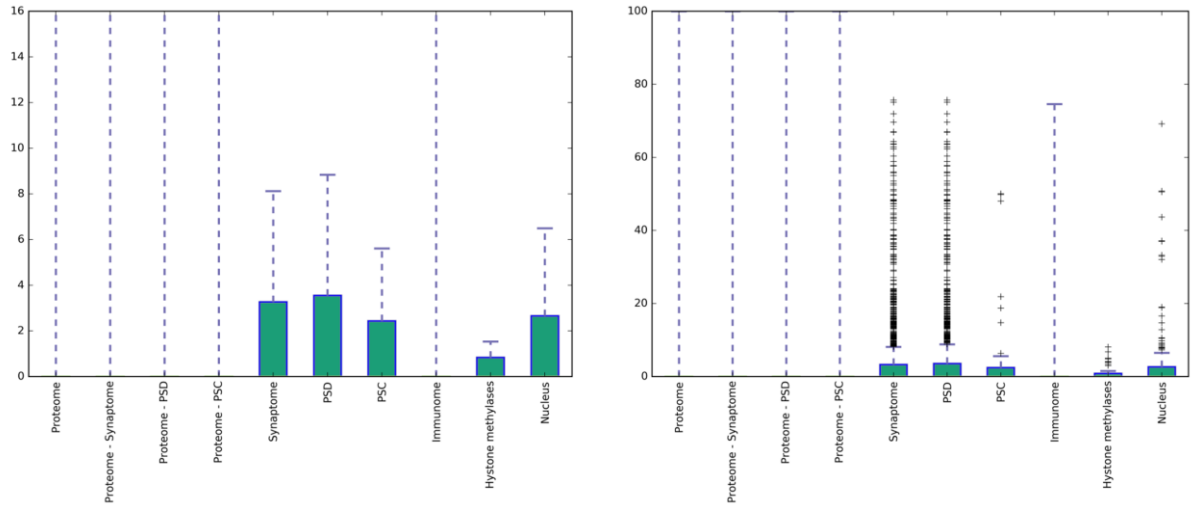

Figure S8: Boxplot of coiled-coil residue content in all datasets (left: without data points; right: with outlier data points. Note the different y-axes).

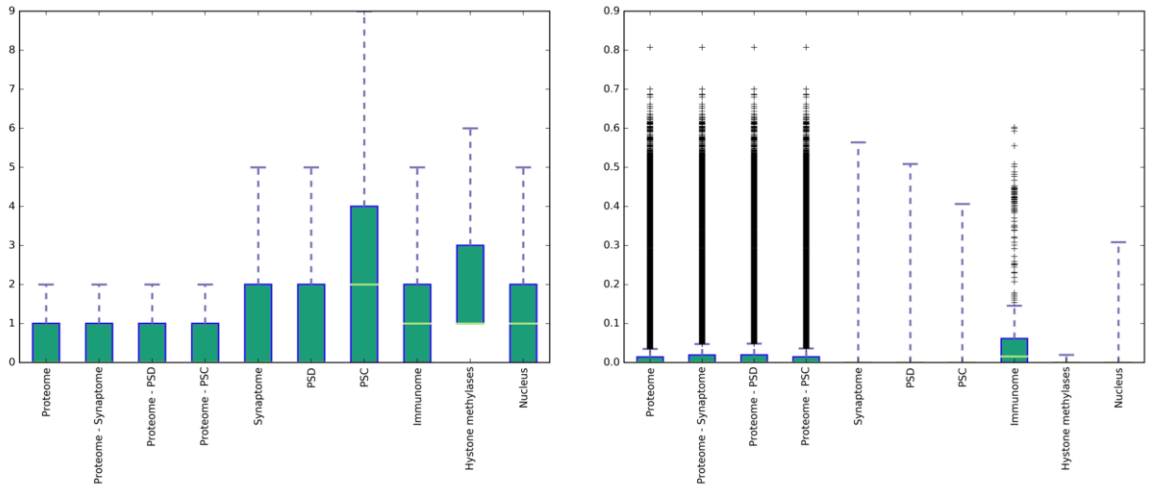

Figure S9: Boxplot of transmembrane residue content in all datasets (left: without data points; right: with outlier data points. Note the different y-axes).

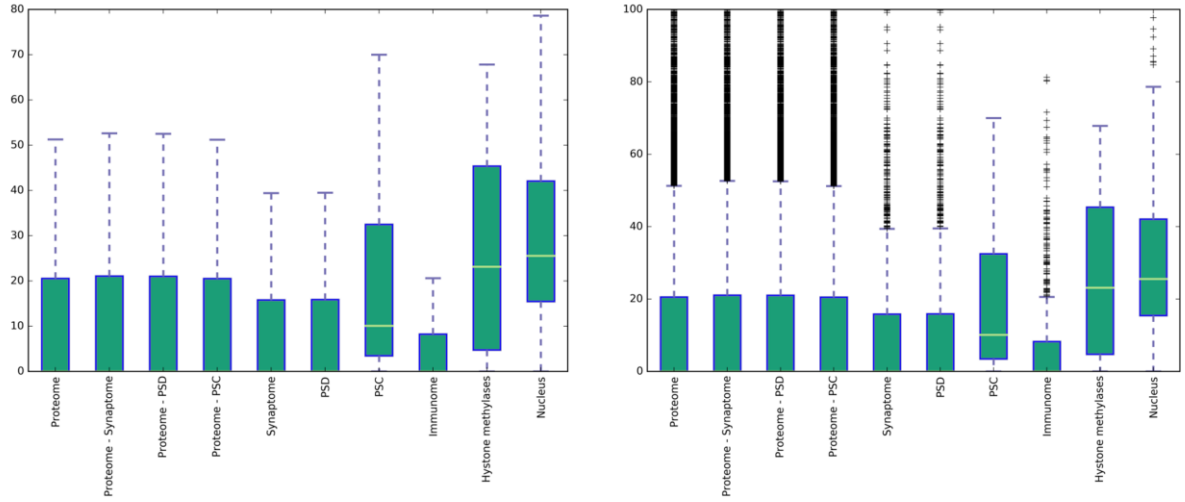

Figure S10: Boxplot of the number of globular domains in all datasets (left: without data points; right: with outlier data points. Note the different y-axes).

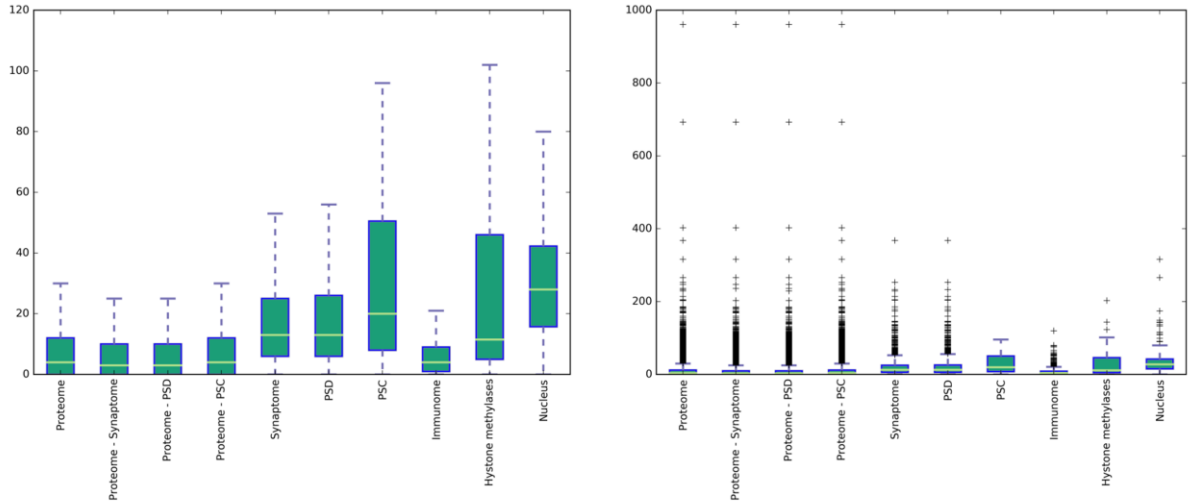

Figure S11: Boxplot of the number of phosphorylation sites in all datasets (left: without data points; right: with outlier data points. Note the different y-axes).

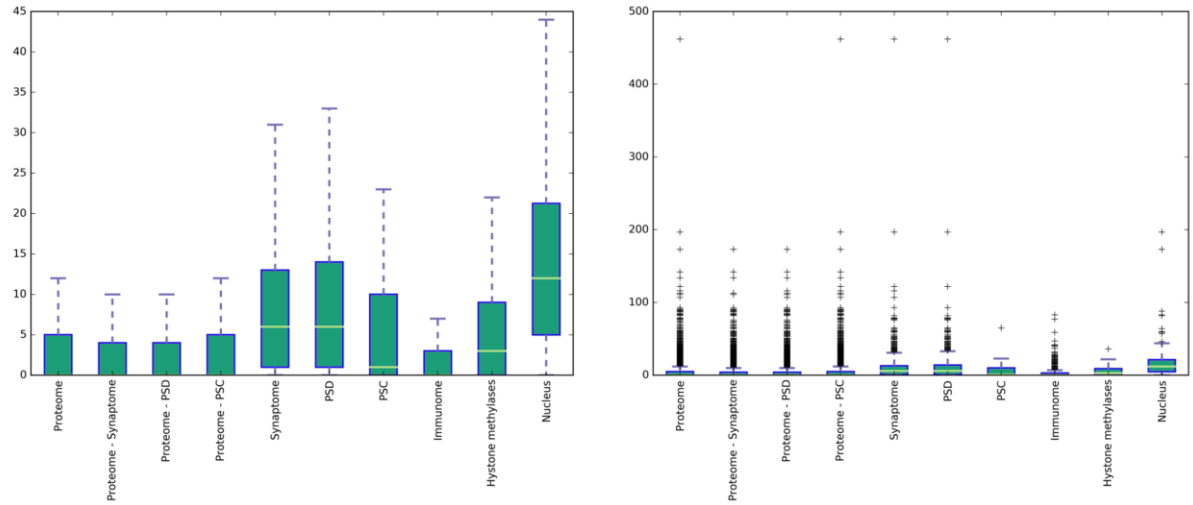

Figure S12: Boxplot of the number of ubiquitination sites in all datasets (left: without data points; right: with outlier data points. Note the different y-axes).

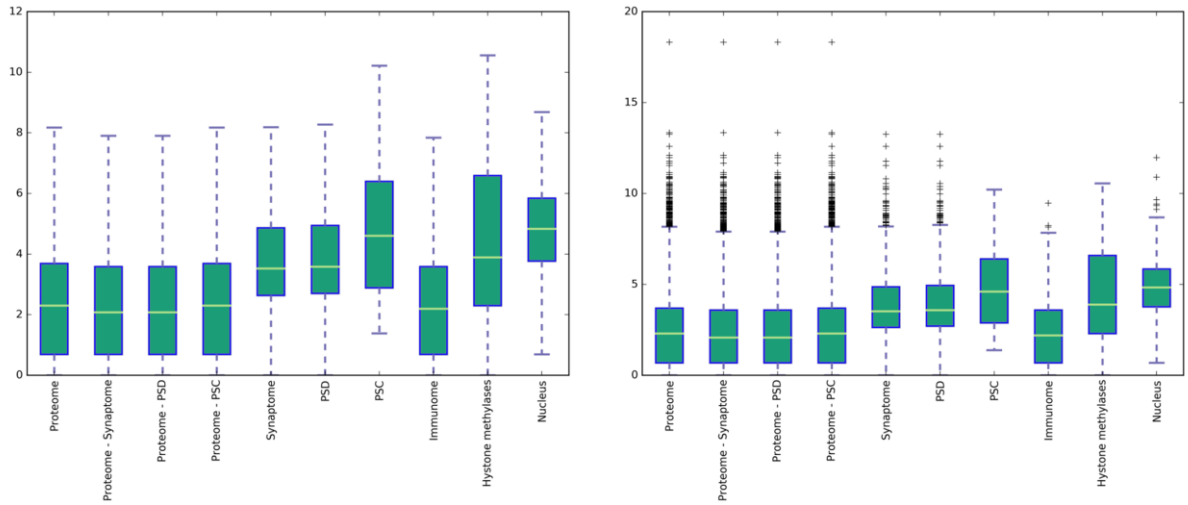

Figure S13: Boxplot of DPI values in all datasets (left: without data points; right: with outlier data points. Note the different y-axes).

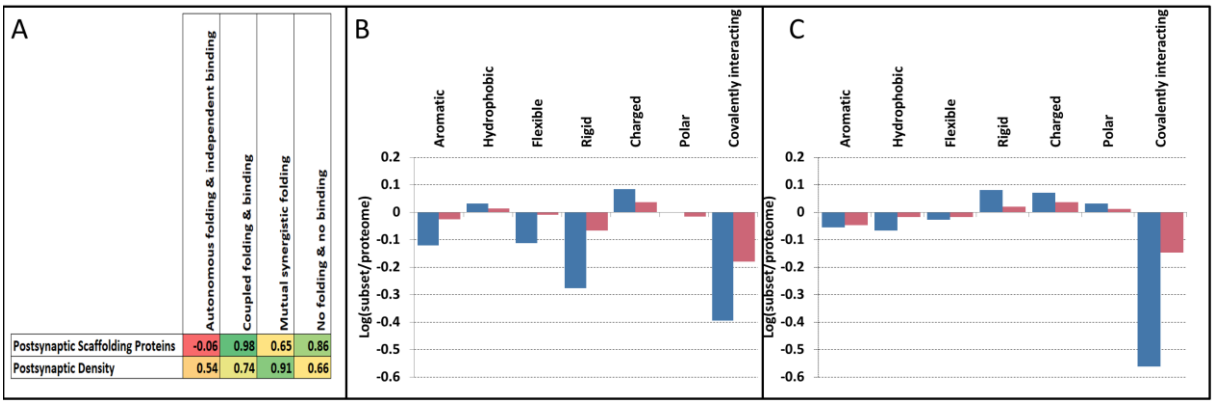

Figure S14: A: Correlation of amino acid content between interaction classes based on the structural state of participating partners and postsynaptic proteins. Columns: Autonomous folding and independent binding (i.e., the binding of two or more ordered proteins), coupled folding and binding (where an ordered protein stabilize an IDP partner) and mutual synergistic folding (interactions formed exclusively by disordered proteins), No folding, no binding (i.e., the “classical” disordered definition). Rows: Postsynaptic Scaffold proteins, and proteins from the postsynaptic density. Color scales from red (negative correlation) to green (positive correlation). B: Change of amino acid content of the group mutual synergistic folding (blue) and PSD proteins (red) compared to the proteome. C: Change of amino acid content of the group coupled binding and folding (blue) and PSC proteins (red) compared to the proteome.

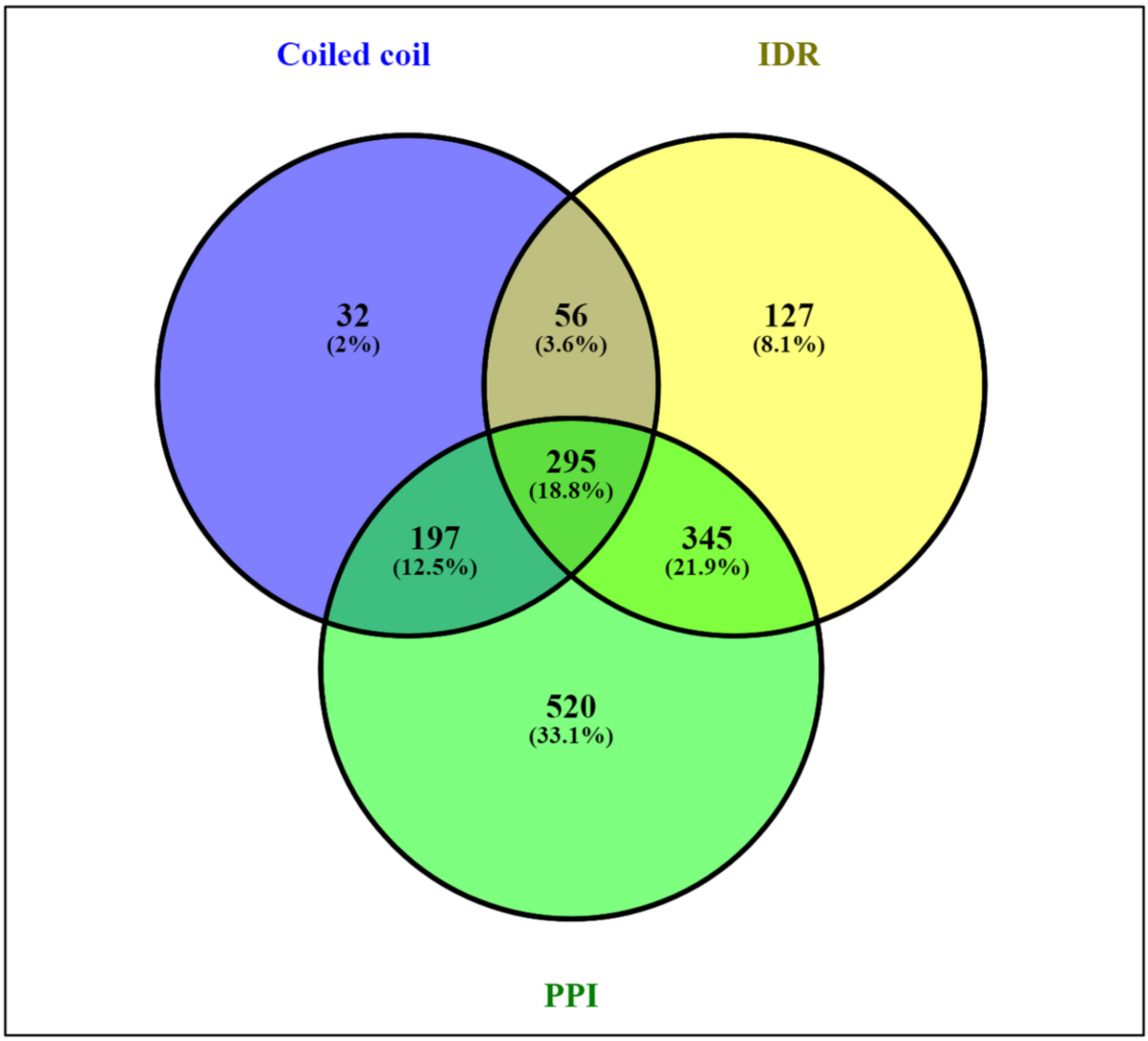

Figure S15: Overlap of coiled coils, IDRs and PPIs in PSD proteins.

Supplementary References

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